Gastrointestinal Tract Dysfunction & Obesity

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Learning Objectives

- Understand common GI disorders that arise from disturbance of physiology
- Appreciate in clinical case scenarios the application of physiology, systems biology and human structure
- See the connection from textbook to patient
- Whet your appetite to learn!
Functions of the GI Tract

• Ingestion of food, Digestion, Absorption and Excretion
  ▪ Mouth, Pharynx, Oesophagus, Stomach, Small & Large Bowel

• Metabolism
  ▪ Liver, Pancreas

• Synthesis
Normal & Disordered GI Function

Normal function
PHYSIOLOGY

Disordered function
PATHOPHYSIOLOGY

HEALTH

DISEASE

SYMPTOMS
Some Common GI Disorders:

- Dysphagia
- Gastric Ulcers and bleeding
- Derangements of gastric acid secretion
- Malabsorption
- Jaundice, gallstones
- Liver failure
- Constipation and colon obstruction
- Obesity
Normal functions

- Saliva (ptyalin, anti-bacterial factors)
- Taste
- Mastication

Disordered function
Normal functions

- Saliva (ptyalin, anti-bacterial factors)
- Taste
- Mastication

Disordered function

- Xerostomia & dental caries
- Ageusia
- Problems with chewing (edentulous, stroke, etc)
Normal & Disordered GI Function

**OESOPHAGUS**

**Normal functions**
- Swallowing
- Peristalsis
- Sphincter relaxation

**Disordered function**
- Dysphagia
- Aperistalsis
- Achalasia
Case Scenario

A 72 year old woman presents in the hospital clinic complaining of difficulty in swallowing for the past 4 weeks. She has trouble swallowing food or drink. She feels food gets ‘stuck’ and reports regurgitation of meals.

- What is the cause?
- How would you find out?
- How would you treat this?
Recognize the altered physiology

**DYSPHAGIA**

“Difficulty in swallowing”

A *symptom*, *not a disease*

*Need to establish* cause
CAUSES OF DYSPHAGIA

OROPHARYNGEAL DYSPHAGIA
- Neuromuscular diseases, eg CVA, Parkinson’s disease
- Local mechanical lesions, eg neoplasm, pharyngeal mass
- Upper esophageal sphincter (UES) disorders

ESOPHAGEAL DYSPHAGIA
- Intrinsic Mechanical lesions, eg carcinoma or stricture
- Extrinsic mechanical lesions, eg vascular compression by vascular abnormality or mediastinal mass.
- Motility disorders, eg achalasia
Imaging
Endoscopy
Normal & Disordered GI Function

**STOMACH**

**Normal functions**
- Secretion of acid, pepsin, IF
- **Gastric mucus** & mucosal barrier
- Storage of food & controlled release into duodenum

Relaxation

**Disordered function**
- Disorders of acid secretion
- Gastric ulcers
- Dumping
- Gastroparesis
- Pyloric stenosis & vomiting
Case Scenario

A 55 year old man presents at the hospital Emergency Dept with vomiting of blood. He also has passed black tarry stools twice in the past 24 hours. He feels faint. He is pale and his blood pressure is 90/50 mm Hg.

• What is the cause?
• How would you treat him?
Recognize the altered physiology

- **vomiting of blood, black tarry stools**
  - break in mucosal barrier with vascular compromise

- **feels faint. He is pale and his blood pressure is 90/50**
  - hypotension, due to blood loss
Gastric Mucosal Barrier

Defending Factors

- Acid/pepsin
- Mucosal-bicarbonate barrier
- Surface phospholipids
- Physical barrier
- pH 2
- Lumen
- HCO₃⁻ secretion
- Cells
- Cell migration/regeneration
- Mucosal prostaglandins
- Mucosal blood flow
Endoscopy
Actively Bleeding Gastric Ulcer
Gastric Ulcer
What Causes Peptic Ulcers?

Attacking Factors:
- Acid
- Pepsin
- NSAIDS
- H pylori

H pylori

Acid, Pepsin

NSAIDS
Helicobacter pylori
Normal & Disordered GI Function

**STOMACH**

**Normal functions**

- **Gastric Secretion**
  - acid, pepsin, IF
- Gastric mucus & mucosal barrier
- Storage of food & controlled release into duodenum
  - peristalsis
  - pyloric sphincter relaxation

**Disordered function**

- Disorders of acid secretion
- Gastric ulcers
- Dumping
- Gastroparesis
- Pyloric stenosis & vomiting
Secretion of HCL by the Parietal Cell

- Chloride (Cl⁻) enters the cell.
- Hydrogen ions (H⁺) are pumped out by the H⁺ K⁺ ATPase.
- Sodium ions (K⁺) enter the cell.
- Carbonic anhydrase catalyzes the reaction: H₂O + CO₂ → H₂CO₃ → H⁺ + HCO₃⁻.
- H⁺ ions combine with OH⁻ to form water (H₂O).
- HCO₃⁻ ions are secreted into the stomach.
Treatment for Peptic Ulcers

- **Drugs**
  - Proton Pump Inhibitors
  - Histamine-2 Receptor Antagonists (H2RA)

- **Surgery**
  - Repair
  - Partial Gastrectomy
  - Vagotony
Normal functions

• Secretion of acid, pepsin, IF

• Gastric mucus & mucosal barrier

• Storage of food & controlled release into duodenum
  - peristalsis
  - pyloric sphincter relaxation

Disordered function

• Disorders of acid secretion

• Gastric ulcers

• Dumping

• Gastroparesis

• Pyloric stenosis & vomiting
Derangements in Gastric Secretion

1. Anacidity - *Pernicious anemia*
2. Hypoacidity - *Gastric ulcer, Gastric CA*
3. High acid output - *Duodenal ulcer*
4. Very high acid secretion - *Gastrinoma*
Normal functions

- Intestinal enzymes & secretions
- Absorption of nutrients, electrolytes & special nutrients
- Intestinal motility & transit

Disordered function
Sites for intestinal absorption

- Duodenum and proximal jejeunum
  - Fats
  - CHO
  - amino acids
  - minerals
  - vitamins except B12

- Terminal ileum
  Special receptors for B12, bile salts
Normal & Disordered GI Function

SMALL INTESTINE

**Normal functions**

- Intestinal enzymes & secretions
- Absorption of nutrients, electrolytes & special nutrients
- Intestinal motility & transit

**Disordered function**

- Maldigestion
- Malabsorption
- Abnormal transit - obstruction or too rapid
Case Scenario

A 24 year old woman presents to the clinic complaining of loss of weight of 10 kg and diarrhoea, over the past 3 months.

• What is the cause?
• How would you find out?
• How would you treat this?
Malabsorption

• Fat malabsorption
  Steatorrhea
  Deficiency of vitamins A,D,E,K

• Protein malabsorption
  Body wasting, hypoproteinemia,

• Carbohydrate malabsorption
How Would You Detect Malabsorption?

- Faecal fat test 100 gram fat diet for 7 days
- Faeces collected last 3 days
- N< 6 grams fat / day excreted

- May be abnormal in pancreatic, biliary or mucosal disease
How Would You Test Intestinal Absorption?

Xylose Absorption test

- 25 g oral dose
- Urine collected for 5 hours (N> 5 g xylose excreted)
- Measure Serum Sample at 90 mins (N> 2 mmol/L)

Abnormal in jejeunal mucosal disease
Mucosal Biopsy
Causes of Malabsorption

Defects of luminal digestion
- Inadequate lipolysis
- Decreased conjugated bile salts

Defects of mucosal cell transport
- Non-specific (tropical sprue, celiac dis)
- Specific eg disaccharidase deficiency

Defects of fat transport in intestinal lymphatics
Normal & Disordered GI Function

Liver & Biliary system

Normal functions

- Bile
- Bilirubin excretion
- Liver functions

Disordered functions

- Fat maldigestion & malabsorption
- Jaundice
- Liver failure
Case Scenario

A 62 year old man presents at the hospital clinic with jaundice which was noticed for one week. He also has tea-coloured urine.

• What is the cause?
• How would you confirm this?
• How would you treat this?
CAUSES OF JAUNDICE

- red cells → haemolysis → unconjugated bilirubin
- Gilbert's syndrome:
  - liver
  - metastatic disease
  - gall stones
  - gall bladder
- cirrhosis, hepatitis, drugs
- chronic pancreatitis
- cancer of pancreas
- duodenum
- pancreas
Gallstones

10-20% of the population

**Calcium bilirubinate stones**
Deconjugation of conjugated bilirubin in bile - >free bilirubin combines with calcium-> insoluble

**Cholesterol stones**
Altered proportions of cholesterol, lecithin and bile salts
Ampulla of Vater: Major papilla

Cannulation of Major papilla

Cholangiogram
Normal functions

- Bile
- Bilirubin excretion
- Liver functions

Disordered functions

- Fat maldigestion & malabsorption
- Jaundice
- Liver failure
Functions of the liver

- Formation of bile
- Carbohydrate metabolism
- Detoxification of drugs, toxins
- Urea & amino acid metabolism
- Production of plasma proteins
- Deconjugating steroid hormones

Liver Failure

- Jaundice
- Hypoglycaemia
- Hepatic encephalopathy
- Muscle wasting
- Hypoalbuminemia
- Oedema, coagulopathy
- Gynecomastia
- Infections / sepsis
- Renal failure
Case Scenario

A 56 year old female is seen in the hospital clinic. She has jaundice, bruises, and swelling of the abdomen and legs. She complains of tiredness, easy fatiguability and confusion.

• What is the cause?
• How would you confirm this?
What is the disordered physiology here?
Functions of the liver

- Formation of bile
- Carbohydrate metabolism
- Detoxification of drugs, toxins
- Urea & amino acid metabolism
- Production of plasma proteins
- Deconjugating steroid hormones

Liver Failure

- Jaundice
- Hypoglycaemia
- Hepatic encephalopathy
- Muscle wasting
- Hypoalbuminemia, oedema, coagulopathy
- Gynecomastia
- Infections / sepsis
- Renal failure
Liver Architecture
Liver Cirrhosis

Liver cirrhosis is a **diffuse** process involving loss of normal liver architecture due to **fibrosis** and **nodule** formation, as a result of hepatocellular necrosis. It implies **irreversible** liver disease.
Cirrhotic liver
Causes of Cirrhosis

• Infections
  – Hepatitis B
  – Hepatitis C

• Toxins
  – Alcohol
  – Organic solvent, benzenes

• Metabolic Disorders
  – Wilson’s Disease
  – Fatty Liver (NASH)

• Autoimmune Conditions
  – Primary Biliary Cirrhosis
  – Autoimmune Hepatitis
Spectrum of Liver Disease in Hepatitis B

- Acute Hepatitis
- **Chronic Hepatitis**
- Chronic liver disease (Cirrhosis)
- **Compensated liver cirrhosis**
- Decompensated cirrhosis
- **Liver failure**
Normal & Disordered GI Function

**COLON**

**Normal functions**
- Absorption of water
- Colonic motility
- Colonic transit

**Disordered function**
- Diarrhoea
- Constipation
- Colonic obstruction & pseudo-obstruction
COLON

Functions

• Absorption of water and Na
• Secretion of K, bicarbonate and mucous
• Storage and propulsion of faeces
• Digestion
Case Scenario

A 68 year old man complains of constipation for the past 3 months. He has difficulty moving his bowels and the stools are small and thin. Previously his usual pattern of bowel movements was once daily. He now presents with a severely distended abdomen and inability to pass motion.

What is the cause?
How would you confirm this?
How would you treat this?
Recognize the altered physiology

- difficulty moving his bowels and stools small and thin = slow transit ? obstruction
- Previously his usual pattern of bowel movements was once daily = a change
- severely distended abdomen and inability to pass motion = obstruction
Colonoscopy
X-Ray
Intestinal obstruction

Failure of transit
  – Distension, pain, constipation, vomiting

Net secretion of fluid and electrolytes
  – Dehydration and electrolyte imbalance

Bacterial translocation
  – Sepsis
Intestinal Obstruction

- Extrinsic: Something from outside the intestine
- Intrinsic: Something inside the lumen
Transit

mouth to caecum - 6 hours
transit through colon - 36 hours
liquid contents in right colon
solid stool in left colon
propulsion in sigmoid
storage and defaecation in rectum
Too FAST = Diarrhoea

Key symptoms

- Loose or watery stools
- 3 or more bowel movements a day
- Stool weight > 200g/day

- **ACUTE:** 1.5% of adult hospitalisations
- **CHRONIC:** 5% of population
Too SLOW = Constipation

Key symptoms

- Hard or lumpy stools
- <3 bowel movements a week
- Straining to defecate
- Sensation of anorectal obstruction
- Manual manœuvreurs to evacuate stool
Stool form also affected by transit

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Separate hard lumps, like nuts</td>
</tr>
<tr>
<td>Type 2</td>
<td>Sausage-like but lumpy</td>
</tr>
<tr>
<td>Type 3</td>
<td>Like a sausage but with cracks in the surface</td>
</tr>
<tr>
<td>Type 4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>Type 5</td>
<td>Soft blobs with clear-cut edges</td>
</tr>
<tr>
<td>Type 6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>Type 7</td>
<td>Watery, no solid pieces</td>
</tr>
</tbody>
</table>
Obesity

• The new epidemic of plenty
• Energy Imbalance
• Different ways of measuring obesity:
  – Weight
  – Body Mass Index (Height – Weight)
  – Waist circumference
  – Waist Hip Ratio
Energy production

The Energy Balance

Energy production
- Proteins
- Carbohydrates
- Fats
- Oxidation

Energy utilization
- Active ion transport
- Muscle contraction
- Synthesis of molecules
- Cell division and growth

ADP + P<sub>i</sub> → ATP

[Diagram of ATP structure with labels for Adenine, Ribose, and Triphosphate]

[Chemical structure of ATP]

[Diagram of ATP cycle with ATP and ADP reactions]
Lipid transport in the body

Exogenous:
- Dietary lipids
  - Small intestines
  - ApoC's
  - ApoE
  - ApoB
  - Chylomicron
  - Chylomicron remnant
  - LPL
  - FFA
  - Muscle
  - Adipose

Endogenous:
- Bile acids + cholesterol
  - LDLR
  - Liver
  - LDL
  - VLDL
  - IDL
  - LPL
  - FFA
  - Muscle
  - Adipose
  - Peripheral tissues
The global effects of the energy imbalance

Blood Vessels
- Coronary blockage (AMI)
- Strokes

Fatty Liver
- Liver stores the fat
- Fat induces inflammation
- NASH / Cirrhosis

Peripheral FAT deposition
- Obesity
- Insulin Resistance
Common GI Disorders: Summary

- Understand common GI disorders that arise from disturbance of physiology
  - Dysphagia
  - Gastric Ulcers and bleeding
  - Derangements of gastric acid secretion
  - Malabsorption
  - Jaundice, gallstones
  - Liver failure
  - Constipation and colon obstruction
  - Obesity
Are there region-specific public health concerns that can be addressed by modifying the gut microbiota? Do you see a need for epidemiological studies to establish correlations and associations between gut microbial communities and health?

De Filippo et al. Effect of Diet on shaping microbiota, comparative study: PNAS 2010
Stool bacteria composition of children living in 10 cities in Asia

Brain-Gut Talk
Less Effective → More Effective

More Invasive and/or Less Safe:
- Gut-directed Antibiotics
- Loperamide
- Prebiotics
- Probiotics
- Systematic Exclusion Diets
- FODMAP Diet
- Stopping PPIs

Less Invasive and/or Safer
Clostridia Difficile Colitis

Ask yourself.....

- **WHY** .... Am I studying physiology?
- **WHERE** .... Can it be applied?
- **WHAT** .... Happens when physiology gets disordered?
- **WHEN** .... Will I get to apply what I’ve learnt? RIGHT NOW!
Blessed Christmas!

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